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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,767	06/01/2001	Harald Schmidt	VOS-101	7502

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EXAMINER

RAO, MANJUNATH N

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 09/09/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/762,767	SCHMIDT ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Manjunath N. Rao, Ph.D.	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 15 June 2003 .

2a)  This action is **FINAL**.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## **Disposition of Claims**

4)  Claim(s) 1-13 is/are pending in the application.

4a) Of the above claim(s) 9-13 is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 1-8 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on 01 June 2001 is/are: a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)  All b)  Some \* c)  None of:

1.  Certified copies of the priority documents have been received.
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)  The translation of the foreign language provisional application has been received.

15)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)  Notice of References Cited (PTO-892) 4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_ .  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948) 5)  Notice of Informal Patent Application (PTO-152)  
3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6)  Other: \_\_\_\_ .

**DETAILED ACTION**

Claims 1-13 are currently pending in this application.

***Election/Restrictions***

Applicant's election without traverse of Group I, claims 1-8 in Paper No. 9 is acknowledged.

***Priority***

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

***Information Disclosure Statement***

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

***Drawings***

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

***Sequence Compliance***

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that applicants fail to provide appropriate SEQ ID NO to sequences cited in the specification, for example see pages 15-16 and 20. See particularly 37 CFR 1.821(d).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase "apparent homogeneity". While the literal meaning of the phrase is clear to the Examiner, the meaning of the above phrase in the context of the above claim is not clear to the Examiner. Specifically the metes and bounds of the above phrase is not clear to the Examiner. A perusal of the specification also does not provide a specific definition for the above phrase. It is not clear to the Examiner as to what extent of purity is considered by the applicant as "apparent homogeneity".

Claims 1 and 6-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 6 recite the phrase "guanylyl cyclase  $\alpha$  1 (hsGC  $\alpha$ 1; SEQ ID NO:2)/ $\beta$ 1 (hsGC  $\beta$ 1; SEQ ID NO:4)". It is not clear to the Examiner as to whether applicants

are claiming the polypeptide as a heterodimer comprising both  $\alpha$  and  $\beta$  subunits or separately as either  $\alpha$  subunit or  $\beta$  subunit.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Giuili et al. (FEBS Lett, Vol. 304(1):83-88). This rejection is based upon the public availability of a printed publication more than one year prior to the date of application for patent in the United States. Claim 1 of the instant application is drawn to isolated human soluble gluanylyl cyclases  $\alpha$  1 or  $\beta$  1 subunits having the amino acid sequences SEQ ID NO:1 and 4 respectively purified to apparent homogeneity. Giuili et al. disclose isolated human soluble gluanylyl cyclases  $\alpha$  1 or  $\beta$  1 subunits having the amino acid sequences SEQ ID NO:1 and 4 respectively purified to apparent homogeneity. Thus Giuili et al. anticipate claim 1 of this application as written.

Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being anticipated by Zabel et al. (Biochem J., Vol. 335(1):51-57, 1998). This rejection is based upon the public availability of a printed publication in the United States. Claims 1 and of the instant application is drawn to isolated human soluble gluanylyl cyclases  $\alpha$  1 or  $\beta$  1 subunits having the amino acid sequences SEQ ID NO:1 and 4 respectively purified to apparent homogeneity and a method of producing

the subunits by expressing the polynucleotide encoding the subunits in prokaryotic or eukaryotic host cells and obtaining the subunits. Zabel et al. disclose isolated human soluble guanylyl cyclases  $\alpha$  1 or  $\beta$  1 subunits having the amino acid sequences SEQ ID NO:1 and 4 respectively purified to apparent homogeneity as well as a method of making said polypeptides by expressing the polynucleotides encoding said subunits in eukaryotic host cells such as insect cells. Thus Zabel et al. anticipate claims 1 and 2 of this application as written.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 3-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Zabel et al. or Giuili et al. as applied to claims 1 or 2 or 1 and 2 above, and further in view of the common knowledge in the art regarding the methods of affinity chromatography using affinity tags for protein purification. Claims 3-8 are directed to methods of producing soluble human guanylyl cyclases (sGC) wherein the step of obtaining the subunits comprises a lysis of cell followed by affinity chromatography of the cell lysate and subsequent elution of the subunits, wherein the expression vectors contains at least one additional DNA sequence encoding for a domain for the specific chromatography (affinity tag) with appended protease cleavage site, wherein the sGC comprises either or both subunits linked to the tag (as in claim 5-8).

The references of Giuli et al. and Zabel et al. has already been discussed above. Both references provide the cDNA expressing the above protein subunits. Zabel et al. also teach the expression of the proteins in a eukaryotic host cell followed by its extraction by cell lysis. However, both references do not teach the affinity chromatography technique for the purification of the above proteins.

The art is rich in teachings of recombinant protein purification techniques involving tags such as histidine tags. In fact, several commercial protein purification kits with appropriate kits are available in the art for those interested in making purified recombinant proteins.

Therefore, with the cDNA for the above sGC enzyme provided by the above two references it would have been obvious to those skilled in the art to subclone the cDNAs provided by the two references in any convenient expression systems which make use of tagged sequences and produce the polypeptides as claimed in claims 3-8. One of ordinary skill in the art would have been motivated to do so as both the above references teach the important role played by the enzyme in signal transduction. One of ordinary skill in the art would have a reasonable expectation of success since the above two references provide a cDNA and the art provides mechanisms to make and express the polypeptide as required.

Therefore, the above invention would have been *prima facie* obvious to one of ordinary skill in the art.

### ***Conclusion***

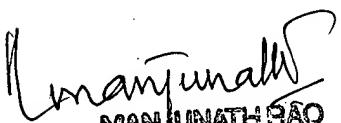
None of the claims are allowable.

Art Unit: 1652

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

  
MANJUNATH RAO  
PATENT EXAMINER  
Manjunath N. Rao  
August 26, 2003